Remarks:

After entry of the amendment, claims 1-13 and 16-25 are pending.

Claims 26-169 have been cancelled to comply with the restriction requirement. Applicants retain the right to divisional or continuation applications directed to the non-elected subject matter.

Claims 1-13 and 16-22 have been amended to recite "sustained release oral formulation" and are supported by, for example, claim 14 and the specification at, for example, page 30, lines 18-23, page 31, lines 16-32, and page 34, lines 9-17. In view of the amendments claims 14 and 15 have been cancelled and the dependency of claim 16 has been amended.

Claim 16 has been editorially amended.

No issues of new matter should arise and entry of the amendment is respectfully requested.

I. Information Disclosure Statement

Applicants thank the Examiner for considering the IDS filed on October 20, 2003. As requested by the Examiner the IDS is being re-filed concurrently.

II. Rejection under 35 U.S.C. §103

Claims 1-25 are rejected under 35 U.S.C. §103 as being unpatentable over Birch et al. (U. S. Patent No. 5,627,191) in view of Cohn (U. S. Patent No. 4,868,179) and Chobanian et al (U. S. Patent No. 5,645,839).

Applicants respectfully traverse the rejection and respectfully submit that the claimed invention is unobvious over the cited references and there is no motivation to combine the cited references to arrive at the presently claimed invention. Applicants respectfully submit that the cited references, individually or in combination, do not disclose or suggest, or provide motivation to arrive at the presently claimed invention.

Birch describes a method for treating a cardiovascular disease, such as, hypertension, by administration of an angiotensin II antagonist of formula I-IV (Birch at Abstract and column 32, line 25-36). At column 33, line 56 to column 34, line 7, Birch states (Emphasis Added):

> In the compositions of the present invention the active compound [i.e., angiotensin II antagonist] may, if desired, be associated with other compatible pharmacologically active ingredients, for example, a β-adrenoceptor antagonist such as atenolol, propranolol, oxprenolol, nadolol

> or timolol, and/or diuretic such as bendrofluzide, ethacrynic acid or frusemide, and/or an angiotensin converting enzyme inhibitor such as captopril or enalapril, and/or vasodilators such as ***hydralazine hydrochloride***, flosequinan, sodium nitroprusside, glyceryl trinitrate or molsidomine, and/or potassium channel activators such as lemakalim or pinacidil, and/or an α-adrenoceptor antagonist such as prazosin or labetalol, and/or other hypotensives such as chonidine, diazoxide, α-methyldopa or ketanserin, and/or positive inotropes such as milrinone, digitalis or dobutamine, and/or PDE inhibitors such as zaprinast, and/or specific bradycardiac agenst such as alinidine or falipamil, an endothelin antagonist and/or an endothelin converting enzyme inhibitor, and/or a rennin inhibitor, and/or a thrombolytic agent such as stoptokinase.

Birch provides a laundry list of compounds that may be used in combination with an angiotensin II antagonist – one of which happens to be hydralazine hydrochloride. Contrary to the Examiner's assertion, Birch does not disclose the amount of hydralazine hydrochloride in the disclosed composition. Birch at column 34, lines 8 – 42, is referring solely to the compounds of Formula I to VI (see definition of the term "active compound" at, for example, column 32, lines 63-64).

Birch's laundry list of compounds does not provide any motivation or suggestion to include isosorbide dinitrate and/or isosorbide mononitrate in the composition. As pointed out by the Examiner, Birch does not even disclose isosorbide dinitrate. Moreover Birch does not provide any motivation for a sustained release oral formulation comprising an antioxidant (e.g., hydralazine) and isosorbide dinitrate as Birch does not even disclose isosorbide dinitrate and isosorbide mononitrate.

Cohn discloses compositions comprising hydralazine hydrochloride and isosorbide dinitrate and/or isosorbide mononitrate. Cohn does not disclose or suggest the sustained release oral formulations of the present invention.

There is no motivation to combine Birch and Cohn to arrive at the claimed invention. Neither Birch nor Cohn provides any motivation for a sustained release oral formulation comprising an antioxidant (e.g., hydralazine) and isosorbide dinitrate and/or isosorbide mononitrate.

Chobanian is cited as teaching transdermal patches. Chobanian does not disclose or suggest sustained release **oral** formulations. Moreover, Chobanian does not disclose or suggest sustained release **oral** formulations comprising at least one antioxidant and at least one of

isosorbide dinitrate and isosorbide mononitrate. There is nothing in Chobanain that would motivate one to make sustained release **oral** formulations comprising at least one antioxidant and at least one of isosorbide dinitrate and isosorbide mononitrate

In view of the above, Applicants respectfully submit that the presently claimed invention is unobvious over the cited references alone or in combination, and respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

III. Conclusion

Applicants respectfully request reconsideration and allowance of claims 1-13 and 16-25.

Examiner Srivastava is encouraged to contact the undersigned concerning any questions about the present application.

Respectfully submitted,

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Dated: October 17, 2006
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